Warfarin

Overview

Over-anticoagulation is common with warfarin therapy. Deliberate OD management depends on whether previously on warfarin and whether bleeding present.

Toxic mechanism

Warfarin inhibits Vit K metabolism reducing the active form needed for synthesis of coagulation factors II, VII, IX & X (& Proteins C & S). Delay of anticoagulation action due to of existing factors. Peak effect is at 72hrs.

Toxicokinetics

Warfarin 100% oral bioavail. Small Vd and highly protein bound. Hepatic met by CP450 + enterohepatic circulation. Excreted in urine & faeces with $T\frac{1}{2}$=35h.

Clinical features

May be asymptomatic or have bruising, or bleeding from gums, nose, in urine etc.

Investigations

Screening: ECG, paracetamol, BSL
Specific bloods: serial INR (@6h, 48h if warfarin naive or q6h if on warfarin)

Risk assessment

INR>5 bleeding risk increases progressively.
Active bleeding = emergency & immediate Rx required.
If not on warfarin: OD<0.5mg/kg likely to be benign. OD>2g/kg significant ↑INR within 72h.

Management

Resus: ABCs if signs of active bleeding. Active uncontrollable bleeding should receive: **prothrombin complex concentrate** (25-50IU/kg) and **FFP** (150-300ml if the prothrombin complex conc given, else 10ml-15ml/kg) IV and **vitamin K** 5-10mg IV.
Supportive Care
Decontamination: Charcoal if <1hr post-OD and already on warfarin.
Antidote: **Vitamin K** (see Antidotes)

Disposition

If warfarin naive & no bleeding, give vit K PO if OD>0.5mg/kg d/c ± INR check @ 48hrs.
If on warfarin admit for serial INR / vitamin K.

Notes

Over warfarinisation is treated as:

1) Therapeutic range<INR<5.0 & no bleeding: ↓dose or omit next dose. Resume at 10-20% lower dose when INR approaches therapeutic range.
2) INR 5.0-9.0 & no bleeding: Cease warfarin, if bleeding risk high, give vit K1 (1.0-2.0 mg PO or 0.5-1.0 mg IV). Measure INR within 24hrs, resume warfarin at 10-20% lower dose once INR is therapeutic.
3) INR >9.0 & no bleeding: Cease warfarin, give 2.5-5.0 mg vitamin K1 PO or 1.0 mg IV. Measure INR in 6-12 hours, resume warfarin at 20% lower dose once INR < 5.0. If high risk of bleeding‡, then give 1.0 mg vitamin K1 IV & consider prothrombin complex concentrate (25-50 IU/kg) and FFP (150-300 mL).
NB. If INR overcorrected and INR<therapeutic range give clexane 1.5mg/kg/day SC until INR>2.0
4) If any clinically significant bleeding: Cease warfarin therapy, give 5.0-10.0 mg vitamin K1 IV, as well as prothrombin complex concentrate (25-50 IU/kg) and fresh frozen plasma (150-300 mL or 10-15ml/kg if no prothrombin complex concentrate), assess patient continuously until INR < 5.0, and bleeding stops.

‡Bleeding risk factors: Age>65, uncontrolled HT, CVA, PUD, IBD, platelets<50, antiplatelet Rx, NSAIDs, recent surgery, renal impairment, recent trauma, EtOH++, liver disease.